

Preliminary Amendment

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Applicant(s): *Dominic E. Cosgrove*Serial No.: *09/970,318*Confirmation No.: *1885*Filed: *October 3, 2001*For: *IMMUNODIAGNOSTIC DETERMINATION OF USHER SYNDROME TYPE IIA***Remarks**

The Examiner is asked to enter the above amendments to the specification. These amendments simply correct typographical errors and add no new matter to the specification.

The amendment made on page 2, line 10 was made to correct the spelling of the author's name in the cited document. The journal title, volume number, page number and year of publication were all cited correctly, and from this information, the correct spelling of the author's name could easily be found.

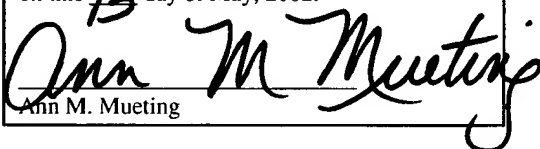
The amendment made on page 37, line 11 was made to complete the journal title in the cited document. Part of the journal's title, the author's name, volume number, page number and year of publication were all cited correctly, and from this information, the complete journal title could easily be found.

Conclusion

The Examiner is invited to contact Applicant's Representatives at the below-listed telephone number, if there are any questions regarding this Preliminary Amendment or if prosecution of this application may be assisted thereby.

CERTIFICATE UNDER 37 C.F.R. 1.8:

The undersigned hereby certifies that this paper is being deposited in the United States Postal Service, as first class mail, in an envelope addressed to: Assistant Commissioner for Patents, P.O. Box 2327, Arlington, VA 22202, on this 13 day of May, 2002.


Ann M. Muetting

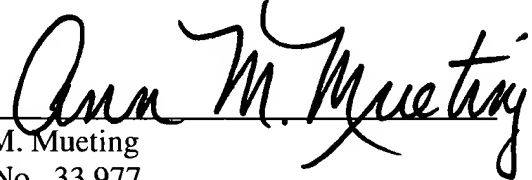
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**APPENDIX A - SPECIFICATION/CLAIM AMENDMENTS
INCLUDING NOTATIONS TO INDICATE CHANGES MADE**

Applicant(s): Dominic E. Cosgrove

Serial No.: 09/970,318

Confirmation No.: 1885

Filed: October 3, 2001

For: IMMUNODIAGNOSTIC DETERMINATION OF USHER SYNDROME TYPE IIA

Amendments to the following are indicated by underlining what has been added and bracketing what has been deleted. Additionally, all amendments have been shaded.

In the Specification

The paragraph beginning at page 2, line 1, has been amended as follows:

Usher syndrome Type II is the most common of the three Usher syndromes. Although originally it was believed that Usher Type II accounted for only about 10% of all Usher cases, more recent research shows that Type II actually accounts for over half of all Usher cases. The USH2A gene has been localized to chromosome 1q41 between D1S474 and AFM144FX2 (Kimberling et al., *Am. J. Hum. Genet.*, 56:216-223 (1995); Sumegi et al., *Genomics*, 35:79-86 (1996)), and more recently, the gene has been identified (Eudy et al., *Science*, 280:1753-1757 (1998)). However, there are Usher Type II families whose disease locus cannot be linked to the 1q41 region. Two new Usher II loci have been localized to 3p and 5q (~~[Pieke-Dahl]~~ ~~Pieke-Dahl~~ et al., *J. Med. Genet.*, 37:256-262 (2000); Hmani et al., *Eur. J. Hum. Genet.*, 7:363-367 (1999)). These new genes have been given the designation USH2B and USH2C, leaving USH2A to refer to the original 1q41 locus.

The paragraph beginning at page 37, line 1, has been amended as follows:

Identification of Tissues that Express Usherin mRNA and Protein.

Usherin is a large glycoprotein with a predicted molecular weight of 170-180 kilodaltons (Eudy et al., *Science*, 280:1753-1757 (1998)). The basic structure of

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the molecule is illustrated in Figure 1. This figure denotes the peptides used as immunogens for the production of antibodies used in these studies, and the portions of the molecule expressed as domain-specific fusion peptides for the protein-protein interaction studies presented. The leader peptide is followed by a 300 amino acid domain with no identifiable homologies. The next 200 amino acids comprise an LN module with homology to LN domains found in the laminin family of basement membrane glycoproteins (Bruch et al., *Eur. J. Biochem*, 185:271-279 (1989), Yurchenco et al., *J. Biol. Chem.*, 268:17286-17299 (1993)), followed by a 500 amino acid stretch containing 10 LE domains, which are rod-like laminin-EGF-like modules (Bork et al., *Q. Rev. Biophys*, 29:119-167 (1996); Beck et al., *FASEB J.*, 4:148-160 (1990)), arranged in tandem. The LE domains are followed by four repeating units of about 100 amino acids each with structural homology to fibronectin type III domains. Fibronectin type III domains are shared by at least 45 different families of molecules, and are dissimilar at the amino acid level, but have very similar and identifiable tertiary structures (Sharma et al., *EMBO J.*, 18:1468-1479 (1999)).